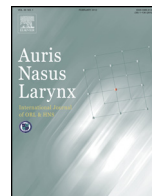




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Complication and surgical site infection for salvage surgery in head and neck cancer after chemoradiotherapy and bioradiotherapy

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ABSTRACT

Objective: We aimed to investigate the complications, surgical site infection (SSI), and survival in salvage surgery without free-flap reconstruction for patients with head and neck squamous cell carcinoma who were treated by platinum-based chemoradiotherapy (Plat-CRT) or cetuximab-based bioradiotherapy (Cet-BRT).

Methods: Thirty-three patients treated by Plat-CRT and six treated by Cet-BRT had salvage surgery. We categorized postoperative complications according to the Clavien–Dindo classification and SSI according to the wound grading scale. Overall survival calculated by Kaplan–Meier method.

Results: Patients with Cet-BRT were significantly associated with the presence of SSI ($P < 0.01$) and grades IIIb–V of the Clavien–Dindo classification ($P < 0.01$) compared with those with Plat-CRT. Patients with Cet-BRT had a significantly lower overall survival than those with Plat-CRT ($P < 0.05$).

Conclusion: We demonstrated that patients with Cet-BRT were significantly more associated with the presence of SSI and grades IIIb–V in the Clavien–Dindo classification than those with CRT.

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1. Introduction

Salvage surgery is radical treatment for recurrence and residual tumor after platinum-based chemoradiotherapy (Plat-CRT) or cetuximab-based bioradiotherapy (Cet-BRT) in head and neck squamous cell carcinoma (SCC) [1]. Complications or surgical site infection (SSI) for many types of surgery including salvage surgery are generally scored using grading systems such as the Clavien–Dindo classification for postoperative complication and the wound grading scale for SSI [2–6]. In our recent study on SSI in head and neck cancer surgery [2], salvage

surgery after Plat-CRT and free-flap procedures were significant risk factors for the presence of SSI, which was assessed by the wound grading scale according to a previous report of Johnson et al. [3].

Recently, Léon et al. reported in 24 patients with head and neck SCC that, in terms of surgical complications after salvage surgery including free-flap reconstruction for recurrence, there were fewer postoperative complications after Cet-BRT than after Plat-CRT, and there was no significant differences in survival after salvage surgery between patients with Plat-CRT and those with Cet-BRT [1]. However, there was no mention for the grades of complication in this study. To the best of our knowledge, SSI had never been compared between Plat-CRT and Cet-BRT, therefore, the complications, SSI and survival have not been fully compared between Plat-CRT and Cet-BRT.

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In Japan, cetuximab has been available for patients with head and neck SCC from December 2012, as described by Sakashita et al. [7]. In this study, we investigated complications, SSI, and survival in salvage surgery without free-flap reconstruction for patients with head and neck SCC who were treated with Plat-CRT or Cet-BRT.

2. Patients and methods

2.1. Patients

Between December 2012 and April 2015, 1202 consecutive patients at the Department of Head and Neck Surgery, Aichi Cancer Center Hospital, received surgical treatment. In terms of the type of surgical treatment, endoscopic surgery and intraoral surgery such as glossectomy and partial maxillectomy were excluded in this study. Of the 1202 patients, a total of 39 patients who both were treated by Plat-CRT or Cet-BRT for head and neck SCC at our institution and received salvage surgery without free flap reconstruction were enrolled in this study. This study was approved by the institutional review board, and all patients provided their informed consent for all treatments and examinations. As classified in our previous article [2], the type of surgical procedure was as follows: 34, neck dissection (ND); 3, total laryngectomy without ND; 1, total laryngectomy with ND; and 1, partial laryngectomy.

2.2. Initial staging

Initial clinical staging was decided by routine physical examination, nasopharyngoscopy, chest radiography, enhanced cervical computed tomography (CT), or magnetic resonance imaging, as well as 18F-fluorodeoxyglucose-positron emission tomography with CT. We performed categorization according to the TNM classification of the International Union Against Cancer (UICC seventh edition).

2.3. Plat-CRT and Cet-BRT

Thirty-nine patients were treated by radical radiotherapy (RT) at a total dose of 60–70 Gy with 2–2.1 Gy per fraction, and all RT procedures have been reported elsewhere [8]. Thirty-three patients treated by concomitant Plat-CRT received one to three cycles of 80–100 mg/m² cisplatin ($n = 13$) on days 1, 21, and 43 of RT, weekly 30 mg/m² cisplatin ($n = 19$), or three cycles of nedaplatin 130 mg/m² on day 5 and 5-fluorouracil at 800 mg/m² day 1–5 ($n = 1$). The total dose of cisplatin for 29 patients who were treated by Plat-CRT including induction chemotherapy, involving the combination of cisplatin and 5-fluorouracil (5-FU), was 287.5 ± 85.2 mg/m². Six patients treated by concomitant Cet-BRT received cetuximab at 400 mg/m² on day 1 of the week preceding RT and a weekly dose of 250 mg/m² cetuximab during RT. The total dose of cetuximab for six patients was 1691.7 ± 534.2 mg/m². For patients who hoped for organ preservation, as described previously [9], we initially recommended Plat-CRT, after which Cet-BRT was used for cases of renal insufficiency or advanced age. At initial treatment, estimated glomerular

filtration rate and age was 86.7 ± 14.9 ml/min/1.73 m² and 59.4 ± 8.2 years in patients with Plat-CRT and 65.3 ± 16.3 ml/min/1.73 m² and 71.5 ± 8.7 years in those with Cet-BRT, respectively.

2.4. Salvage surgery

We performed both preoperative staging (T and N classification, stage) based on the UICC seventh edition and salvage surgery for 19 recurrent and 20 residual tumors. Antibiotics were administered as 1 g of cefazolin for ND alone and 1.5 g of ampicillin-sulbactam for total laryngectomy or partial laryngectomy at the induction of general anesthesia. For total laryngectomy and partial laryngectomy, the same antibiotics were administered at 4 h and two times every 12 h; all surgical procedures for wound have been reported elsewhere [2]. Thirty-nine patients were grouped by surgical procedure: ND alone (ND alone group, $n = 34$) and total laryngectomy with/without ND or partial laryngectomy (primary \pm ND group, $n = 5$).

2.5. Grading

Applying the method described in a previous study, surgical wounds and complications were observed daily until patient discharge; we scored SSI using the wound grading scale developed by Johnson et al. [2,3], and both grade 4 (purulent drainage either spontaneously or by incision and drainage) and grade 5 (orocutaneous fistula) were defined as the presence of SSI [2]. Complications were scored using the Clavien–Dindo classification [4,5]. We counted only complications of grade II or higher because grade I represents only minor deviations from the normal postoperative course, as described previously [4].

2.6. Clinical characteristics and parameters

The clinical characteristics and parameters were recorded for all patients according to their medical charts: initial T and N classification, T and N classification, stage, age, sex, tumor site, diagnosis (recurrence/residual), group of salvage surgery (ND alone/primary \pm ND), smoking, alcohol consumption, past history of operation, induction chemotherapy, preoperative tracheostomy, performance status according to the Eastern Cooperative Oncology Group, radiation dose, Charlson comorbidity index (CCI) which was a weighted index composed of 19 comorbid conditions [10], body mass index, pretreatment laboratory values (leukocytes, hemoglobin, thrombocytes, albumin, estimated glomerular filtration rate), blood loss during surgery, and operation time.

2.7. Statistical analysis

The statistical analysis was carried out using the JMP software package (version 9; SAS; Cary, NC, USA). The relationships between the type of initial treatment (Plat-CRT, Cet-BRT) and clinical characteristics (Initial T and N classification, T and N classifications, stage, age, sex, tumor site, diagnosis, group of salvage surgery, smoking, alcohol consumption, past history of operation, induction chemotherapy,

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